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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/973,674	10/09/2001	Hannes Loferer	GPCG-P01-019	5774
28120	7590	10/01/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			SHAHNAN SHAH, KHATOL S	
			ART UNIT	PAPER NUMBER

1645

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/973,674

Applicant(s)

LOFERER ET AL.

Examiner

Khatol S Shahnan-Shah

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2004 and 25 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-13, 16 and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14, 15, 17 and 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-17 and 19-26 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/25/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment received 07/06/2004 is acknowledged. Claims 14, 15 and 17 have been amended. Claim 18 has been canceled. New claims 22-26 have been added.

Election/Restrictions

2. Applicants' election with traverse of 07/06/2004, is acknowledged. Applicant provisionally elected Group IV claims 14, 15, 17 and 18 which are drawn to use of a polypeptide. The traversal is on the ground that it would not be a serious burden on the examiner to search distinct groups has been noted. This is not found persuasive because while the searches may overlap, they are not coextensive. Applicants also argue that it appears that search for groups I and IV would be coextensive because both these groups are classified in group 435. This is not found persuasive because the groups require different literature searches in view of different method steps.

The requirement is still deemed proper and is therefore made **FINAL**.

Per applicants' request newly added claims 22-26 will be grouped into elected group IV.

3. Currently claims 1-17 and 19-26 are pending.
4. Claims 1-13, 16 and 19-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions.
5. Currently claims 14, 15, 17 and 22-26 are under consideration.

Drawings

6. This application lacks formal drawings. The informal drawings filed in this application are acceptable for examination purposes. When the application is allowed, applicant will be required to submit new formal drawings.

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Information Disclosure Statement

7. Applicants' information disclosure statement of 8/25/04 is acknowledged. The references has been considered by the examiner, see attached PTO form 1449. However, the PALM system list another IDS from 10/1/2003. The PTO 1449 from this IDS is missing from the electronic version of this case, but the references exist in the electronic system. The examiner respectfully requests for a curtsey copy of PTO 1449 from the applicant so those references can be considered.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 14, 15, 17 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP) 2164.01(a).

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples (6) the quantity of experimentation, (7) the relative skill of those in the art, and (8) the breadth of the claims.

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The instant claims are drawn to a method for identifying an antagonist or inhibitor of the activity of a polypeptide, or a fragment, derivative or ortholog thereof. These terms can read on as few as one or more amino acids.

The breadth of the instant claims is drawn to multiple polypeptides, which are not specified in the sequence disclosure. The specification states that the term fragment or derivative further denotes compounds analogous to an antagonist or inhibitor that should have a stabilized electronic configuration (see page 4) however the specification provides no guidance as to what amino acids may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which amino acids could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein's structure/function relationship, e.g. such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions.

It is also unclear how the amino acid sequences are selected or how the skilled artisan would predict the sequences required to accomplish the required function. The specification does not teach how one would make this selection or teach a method to predetermine the sequence structure for appropriate selection to result in the required affinity constant. The art teaches that even minor changes in the amino acid sequences may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function (see abstract and title).

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Substitution of amino acids into a known sequence as well as identifying and using fragments of proteins containing an isolated functional domain of a protein is within the realm of protein chemistry and is one of the most unpredictable areas of protein chemistry. For example Burgess et al. (J of Cell Biology, 1990 Vol. 111, pp.2129-2138) teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Furthermore, Lazar et al (Molecular and Cellular Biology, 1988, Vol. 8, pp. 1247-1252) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

Applicants have provided no guidance to enable one skilled in the art how to determine, without undue experimentation, the effect of different substitutions and the nature and the extend of the changes that can be made. In view of all of the above, in view of the lack of predictability in the art, and lack of guidance on how to obtain the desired fragments and analogs it is determined that it would require undue experimentation to make and/or use the claimed invention. In summary, the actual invention is not described in such a way that one skilled in the art could grasp the invention and make and/or use the invention and/or reproducibly practice the invention with a reasonable expectation of success, without undue experimentation. In the absence of specific guidance and evidence, instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 14, 15, 17 and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14 and 17 are vague and indefinite due to the phrase “or fragments, derivatives or analogues thereof”. A fragment reads on as few as one amino acid. The metes and bounds of the claimed molecule cannot be understood. It is not clear what is encompassed by “or fragments, derivatives or analogues thereof”.

Claims 22, 23, 24 and 26 are vague and indefinite due to the phrase “interaction of said polypeptide molecule with polypeptide” because it is unclear what is the difference between these polypeptides. Clarification is requested.

Claim 25 is indefinite for reciting the phrase “a small molecule”. It is unclear as to what applicants are referring?

Claim 15 is indefinite as being dependent from indefinite claim 14.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on 7:30am-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (571)-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

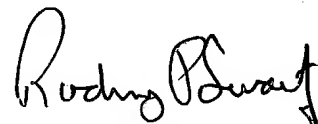


Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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September 27, 2004



RODNEY P. SWARTZ, PH.D.
PRIMARY EXAMINER